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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/869,638	02/08/2002	Tim Wilhelm Nattkemper	HSS-021XX	5891

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EXAMINER	
LAVIN, CHRISTOPHER L	

ART UNIT	PAPER NUMBER
2621	

DATE MAILED: 02/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/869,638	NATTKEMPER ET AL.	
	Examiner	Art Unit	
	Christopher L Lavin	2621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1 – 3, 6 – 12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luck (5,257,182) in view of Watkin ("Minimum Distance Processor for

Biological Tissues Classification From A-Scan Ultrasonic Signals"; IEEE 1995) and Watanabe (5,522,015).

5. In regards to claim 1 Luck discloses a method for analyzing microscope images comprising of the following steps:

a) Taking at least two microscope images of a sample including a plurality of biological objects (col. 4, lines 13 – 19);

b) Selecting a first microscope image and marking the positions (s) of mass gravity centers, i.e., centroids, of a number n of the individual objects discernible in the first microscope image, in which step each marked object is assigned a defined first image excerpt which completely surrounds the marked object, and each first image excerpt including a marked object, and each first image excerpt including a marked object is assigned the value 1, with the number n of such marked first image excerpts constituting a positive training set (col. 7, lines 46 – 53; col. 13, lines 17 – 23: Two training sets are disclosed, malignant and benign with a 0.9 and 0.1. Luck does not disclose using 1 and 0 for training a neural network. This will be shown to be well known in the art through Watanabe below. A complete training set consists of a positive (1) and a negative (0) training set; col. 13, lines 40 – 48: the training set is based on "precisely the same type of net images" as were obtained for classification.);

d) Determining characteristic features and/or feature combinations of the positive and negative training sets and assigning said characteristic features and/or feature combinations to a classification value between 0 and 1, said classification value

representing the degree of probability of the presence of a marked object, and the determined features and/or feature combinations are stored (col. 13, lines 57 – 64);

e) Determine classification values of all image points of the second and each further microscope image by comparing the image data of the second and each further microscope image with the features and/or feature combinations determined in procedural step d), in which step, for each image point of the second and each further microscope image, the classification value for an image excerpt surrounding the image point is determined and the size and shape of this image excerpt corresponds to the size and shape of the first or second image excerpt (col. 13, lines 17 – 23);

Luck does not disclose using minimum distance for classification purposes. Computing distance for classifying images is extremely well known as evidenced by Watkin see third paragraph on page 529.

Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention to use minimum distance for classification in the medical field (as disclosed by Watkin) in the method disclosed by Luck if for no other reason than to classify the medical images correctly.

Luck (as modified by Watkin) does not disclose using 1 and 0 for training a neural network. However, Watanabe (col. 5, lines 59 – 61) discloses using 1 and 0 to train a neural network. Luck discloses a method capable of classifying biological specimens on a microscope slide, however Luck has not specifically claim a threshold. However, Watanabe (col. 25, lines 42 – 44) discloses using a threshold of 0.5 to separate neural network outputs into two possibilities.

Therefore it would have been obvious to one having ordinary skill in the art at the time of the invention to use 0 and 1 to train a neural network as taught by Watanabe instead of 0.1 and 0.9 as taught by Luck (as modified by Watkin). As the intent is to separate two types allowing more separation between the types will allow for better thresholding. Also to use thresholding for classification of neural network outputs (as disclosed by Watanabe) in the method disclosed by Luck (as modified by Watkin) allows for separation of the data into two subsets, as Luck's method is designed to classify a cell as either malignant or benign thresholding will quickly and easily separate outputs for easy analysis.

6. With regards to claim 2, the method as claimed in claim 1 wherein the sample is a tissue sample and the biological object is a cell (Luck, col. 8, lines 33 – 35).

7. With regards to claim 3, the method as claimed in claim 1 wherein the biological objects to be determined are marked with one or plural chemical markers before the microscope images are taken (Luck, col. 8, lines 33 – 35).

8. With regards to claim 6, the method as claimed in claim 1 wherein the microscope images are taken by a CCD camera and then digitized (Luck, col. 7, lines 11 – 13).

9. With regards to claim 7, the method as claimed in claim 1 wherein the number n of the individual biological objects marked in procedural step b) is larger than or equal to 50 (Luck, col. 13, lines 17 –19: As "several hundred or thousands" of cells are used to create a training set inherently at least 50 of these biological objects would represent the positive (malignant) case.).

10. With regards to claim 8, the method as claimed in claim 1 wherein the first image excerpt is of square shape, with the size and/or side length of the first image excerpt corresponding at least to the maximum diameter of the biological objects in the first microscope image (Luck, col. 7, lines 49 – 59).

11. With regards to claim 9, the method as claimed in claim 1 wherein the number n of second image excerpts is larger than or equal to 50, with the second image excerpts being defined automatically, keeping to the minimum distance from the respective first image excerpts (Luck, col. 13, lines 17 – 19: As "several hundred or thousands" of cells are used to create a training set inherently at least 50 of these biological objects would represent the negative (begin) case; Watkin, third paragraph on page 529).

12. With regards to claim 10, the method as claimed in claim 1 wherein classification values of all image points of the second and each further microscope image are automatically determined according to procedural step e) by scanning the image surface of the second and each further microscope image (Luck, col. 14, lines 3 – 7).

13. With regard to claim 11, the method as claimed in claim 1 wherein the threshold value of the classification value representing the presence of a biological object is at least 0.5 (Watanabe, Col. 25, lines 42 – 44).

14. With regards to claim 12, the method as claimed in claim 1 wherein the object positions determined by procedural steps a) to f) are compared in the total number of microscope images so as to obtain a spatial location and distribution of the individual objects in the sample (Luck, col. 14, lines 30 – 35).

15. With regards to claim 14, the method as claimed in claim 2 wherein the biological objects to be determined are marked with one or plural chemical markers before the microscope images are taken (Luck, col. 8, lines 33 – 35).

16. Claims 4, 5, 13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Luck (as modified by Watkin and Watanabe) as applied to claim 3 above, and further in view of Hemstreet (5,733,721).

Luck discloses a method for analyzing a microscope slide containing biological cells (col. 5, lines 16 – 21). Luck however does not teach how to prepare that slide or that fluorochrome should be used to mark the slide.

Hemstreet teaches that slides should be rinsed (col. 28, lines 27 – 32) before staining. Hemstreet then teaches that to create fluorescent images requires staining the slide with a fluorchrome (col. 7, line 64 – col. 8, line 6). Hemstreet then analyzes the fluorescent images with a neural network (col. 7, lines 47 – 51).

Luke (as modified by Watkin and Watanabe) and Hemstreet are combinable because they are from the same field of endeavor, i.e., using neural networks to classify biological cells. It would have been obvious to one having ordinary skill in the art at the time of the invention to prepare and stain the microscope slide (as taught by Hemstreet) before analyzing the microscope slide (as taught by Luke). A slide needs to be prepared in advance of use if the results are to be trusted. By staining the slide the method disclosed by Luke will have an easier time of identifying cells of interest.

17. With regards to claim 4, the method as claimed in claim 3 wherein the objects to be determined are marked with one or plural chemical markers before the microscope

images are taken, with a bleaching or rinsing procedure being performed between the taking of the individual microscope images (Hemstreet, col. 28, lines 27 – 32).

18. With regards to claim 5,the method as claimed in claims 3 wherein said chemical markers are fluorochrome markers and the microscope images are fluorescence images (Hemstreet, col. 7, line 64 – col. 8, line 6).

19. With regards to claim 13, use of a method as claimed in claim 1 for the automatic cell classification of fluorescent cells (Luck, col. 3, lines 38 – 39; Hemstreet, col. 7, line 64 – col. 8, line 6).

20. With regards to claim 15, the method as claimed in claim 4 wherein said chemical markers are fluorochrome markers and the microscope images are fluorescence images (Hemstreet, col. 7, line 64 – col. 8, line 6).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher L Lavin whose telephone number is 703-306-4220. The examiner can normally be reached on M - F (8:30 - 5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Leo Boudreau can be reached on (703) 305-4706. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CLL

DANIEL MIRIAM
PRIMARY EXAMINER